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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,316	10/23/2003	Mu-En Lee	HUV-046.02	8228

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EXAMINER	
MACFARLANE, STACEY NEE	
ART UNIT	PAPER NUMBER
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
31 DAYS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,316	LEE ET AL.	
	Examiner	Art Unit	
	Stacey MacFarlane	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-30* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 2-9, and 21, drawn to method for identifying a gene that regulates proliferation of smooth muscle comprising identifying genes that are up or down regulated, classified in class 536, subclass 23.1.

II. Claims 2-6, 10, 11, and 21, drawn to method of identifying and agent that regulates proliferation comprising contacting cells with a test agent and measuring the ability of the test agent to inhibit differentiation, classified in class 435, subclass 3.

III. Claims 12-14, 21 and 30, drawn to method of identifying an agent comprising identifying a gene product that is up or down regulated AND identifying an agent that inhibits or potentiates the activity of that gene product, classified in class 435, subclass 3.

IV Claims 15-17, 21, drawn to a method comprising identification of an agent that alters that biological activity of latent TGF-β binding protein, classified in class 435, subclass 3.

V. Claims 18, 19, 21, drawn to a method comprising identifying an agent which inhibits the activity of an integrin linked kinase, classified in class 435, subclass 3.

VI. Claims 20, 21, drawn to a method identifying an agent which inhibits a LEF-1/β-catenin signaling pathway, classified in class 435, subclass 3.

VII. Claim 23, drawn to a method of modulating proliferation and/or migration of smooth muscle cells comprising contacting with an agent able to modulate proliferation and/or migration of smooth muscle cells ***in vitro***, classified in class 435, subclass 375.

VIII. Claims 24-27, drawn to drawn to a method of modulating proliferation and/or migration of smooth muscle cells comprising contacting with an agent able to modulate proliferation and/or migration of smooth muscle cells ***in vivo***, classified in class 424, subclass 9.1.

IX. Claims 28 and 29, drawn to a method of treating unwanted proliferation of smooth muscle cells, classified in class 424, subclass 9.1.

2. Claim 1 link(s) inventions of Groups I and II. The restriction requirement between the linked inventions is **subject to** the nonallowance of the linking claim(s), claim 1. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions **shall** be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 **Claims that require all the limitations of an allowable linking claim** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is

earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

3. Claim 22 link(s) inventions of Groups VII and VIII. The restriction requirement between the linked inventions is **subject to** the nonallowance of the linking claim(s), claim 22. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions **shall** be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 **Claims that require all the limitations of an allowable linking claim** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting

rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

4. Inventions of Groups I and II are related as subcombinations disclosed as usable together in a single combination (Group III). The subcombinations are distinct if they do not overlap in scope and are not obvious variants, and if it is shown that at least one subcombination is separately usable. In the instant case, subcombination of Group II has separate utility such as identifying test agents that specifically inhibit differentiation, and the invention of Group I has a separate utility for identifying genes that are involved in differentiation. Furthermore, the two groups do not overlap in scope, Group I encompasses genes that are up- or down-regulated upon differentiation whereas Group II recites agents that specifically inhibit the process. See MPEP § 806.05(d).

The examiner has required restriction between subcombinations usable together. Where applicant elects a subcombination and claims thereto are subsequently found allowable, any claim(s) depending from or otherwise requiring all the limitations of the allowable subcombination will be examined for patentability in accordance with 37 CFR 1.104. See MPEP § 821.04(a). Applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

5. Inventions of Groups III and those of Group I/II are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombinations as claimed. The subcombinations of Groups I/II require, for example, that the neural crest cells be cultured under conditions wherein SM22α is induced, whereas the combination of Group III does not require induction of this gene expression. Furthermore, the subcombinations of Group I and Group II serve separate utilities: as a method for the identification of genes **regulating smooth muscle proliferation**, and a screening method for the identification of agents that **specifically inhibit differentiation**, respectively.

The examiner has required restriction between combination and subcombination inventions. Where applicant elects a subcombination, and claims thereto are subsequently found allowable, any claim(s) depending from or otherwise requiring all the limitations of the allowable subcombination will be examined for patentability in accordance with 37 CFR 1.104. See MPEP § 821.04(a). Applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

6. Inventions of Groups II-VI and the inventions of Groups VII/VIII are related as subcombinations disclosed as usable together in a single combination (Group IX). The subcombinations are distinct if they do not overlap in scope and are not obvious variants, and if it is shown that at least one subcombination is separately usable. In the instant case, subcombinations of Groups II-VI **each** have separate utility: The claimed methods of Group II identify agents that specifically inhibit differentiation; The method of Group III serves to identify agents that specifically inhibit or potentiate the gene products of Group I; Group IV identifies agents that alter the biological activity of latent TGF-β; The method of Group V identifies agents that inhibit the activity of an integrin-linked kinase; Group VI identifies agents that specifically inhibit a LEF-1/β-catenin signaling pathway. The products used in the method of Groups VII and VIII are products-by-process, which reads on any product that modulates proliferation/migration. The products of Group VII have a separate utility of being used in vitro whereas the products of Group VIII have a separate utility in vivo. See MPEP § 806.05(d).

The examiner has required restriction between subcombinations usable together. Where applicant elects a subcombination and claims thereto are subsequently found allowable, any claim(s) depending from or otherwise requiring all the limitations of the allowable subcombination will be examined for patentability in accordance with 37 CFR 1.104. See MPEP § 821.04(a). Applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to

provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

7. Inventions of Group IV-VI are directed to related processes. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed each require identification of an agent with a different functional activity: altering latent TGF-β binding protein; inhibiting the activity of an integrin linked kinase; or inhibiting a LEF-1/β-catenin signaling pathway. The inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

8. Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

9. Inventions of Groups IV-VI versus I/II are directed to related methods. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed, each require the identification of agents with different

activity (Groups IV-VI) and the methods of Group I/II require culturing methods that specifically induce SM22α gene expression. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

10. Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art due to their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

11. Inventions of Group IV-VI versus Group III are directed to related processes. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed, are materially distinct in design: The method of Group III requires the identification of a product that is up- or down-regulated, whereas the methods of IV-VI require an assessment of an agent's ability to modulate proliferation. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

12. Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required

because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

13. Inventions of Group VII and VIII are directed to related processes. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed are materially distinct in design. The method of Group VII, drawn to in vitro methods, would require very different methodology than the process performed in vivo as in Group VIII. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

14. Inventions of Groups IX versus I-VI and VIII are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed. For example the combination of Group IX, reciting treatment of unwanted proliferation, does not recite the particulars of Groups IV-VI, which require alteration/inhibition of latent TGF-β, integrin-linked kinase, or LEF-1/β-catenin, respectively. Likewise, the combination does not require that neural crest cells be cultured under conditions that induce SM22α gene

expression, as in Groups I and II. Still further, the fact that each of the subcombinations are claimed independently is evidence that the particulars of neither subcombination is required for the patentability of the combination. Furthermore, the subcombinations have separate utility as follows: The method of Group I serves to identify genes that regulate proliferation of smooth muscle cells; Group II identifies agents that specifically inhibit differentiation; Group III identifies agents that specifically inhibit or potentiate the gene products of Group I; Group IV identifies agents that alter the biological activity of latent TGF-β; Group V identifies agents that inhibit the activity of an integrin-linked kinase; Group VI identifies agents that specifically inhibit a LEF-1/β-catenin signaling pathway.

The examiner has required restriction between combination and subcombination inventions. Where applicant elects a subcombination, and claims thereto are subsequently found allowable, any claim(s) depending from or otherwise requiring all the limitations of the allowable subcombination will be examined for patentability in accordance with 37 CFR 1.104. See MPEP § 821.04(a). Applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

15. Inventions of Group IX and VII are unrelated: Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant

case, the different inventions are drawn to inventions that are not disclosed as capable of use together. The methods of Group VII are drawn to in vitro methods for modulation proliferation and/or migration of smooth muscle cells, whereas the methods of Group IX are drawn to treatment in vivo.

16. Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

Species Election

17. This application contains claims directed to the following patentably distinct species:

Group III Only:

Elect **either** potentiates **or** inhibits [for Claim 12 (ii)].

Group IV Only:

Elect **one** of the following gene products: latent TGFI3 binding protein, integrin-linked kinase, aortic carboxypeptidase, a Torsin, cctζ, prothymosin, Limk2, Cca (confluent 3Y1 cell-associated), an interferon activatible protein, intemexin, Caspase, AHNAK, Desmoyokin, TSC-36 (TGF inducible protein), Transcobalamin, a fos-related antigen, an epididymal secretory protein E1 precursor (HE1), a ubiquitin carboxyl-terminal hydrolase, a thyrotropin releasing hormone, **OR** a Decorin.

The species are independent or distinct because they are structurally and functionally distinct genes or gene products mediating different physiological effects within smooth muscle.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not

distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

18. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not

commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

19. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacey MacFarlane whose telephone number is (571) 270-3057. The examiner can normally be reached on Monday-Thursday 6:30AM-4:00 PM & ALT. Fridays, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on (571) 272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DANIEL M. SULLIVAN, PH.D.
PRIMARY EXAMINER